CLAIMS

What is claimed is:

1. An immunomodulatory polynucleotide comprising an immunostimulatory sequence (ISS), wherein the ISS comprises the formula:

5'-X_1 X_2 A X_3 C G X_4 T C G-3' (SEQ ID NO: 62)

wherein X_1 is T, G, C or Z, wherein Z is 5-bromocytosine;

wherein X_2 is T, G, A or U;

wherein X_3 is T, A or C;

wherein X_4 is T, G or U; and

wherein the ISS is not 5'-TGAACGTTCG-3' (SEQ ID NO: 63) or 5'-GGAACGTTCG-3' (SEQ ID NO: 64).

2. An immunomodulatory polynucleotide according to claim 1, wherein the ISS is selected from the group consisting of TGAACGUTCG (SEQ ID NO: 67), TGACCGTTCG (SEQ ID NO: 68), TGATCGGTCG (SEQ ID NO: 69), TGATCGTTCG (SEQ ID NO: 70), TGAACGGTCG (SEQ ID NO: 71), GTAACGTTCG (SEQ ID NO: 72), GTATCGGTCG (SEQ ID NO: 73), GTACCGTTCG (SEQ ID NO: 74), GAACCGTTCG (SEQ ID NO: 75), ZGACCGTTCG (SEQ ID NO: 76), wherein Z is 5-bromocytosine, CGAACGTTCG (SEQ ID NO: 77), CGACCGTTCG (SEQ ID NO: 78), ZGAACGTTCG (SEQ ID NO: 79), wherein Z is 5-bromocytosine, TTAACGUTCG (SEQ ID NO: 82), TUAACGUTCG (SEQ ID NO: 81) and TTAACGTTCG (SEQ ID NO: 80).

3. An immunomodulatory polynucleotide according to claim 2, wherein the ISS is selected from the group consisting of TGAACGUTCG (SEQ ID NO: 67), GAACCGTTCG (SEQ ID NO: 75) and CGAACGTTCG (SEQ ID NO: 77).

4. An immunomodulatory polynucleotide according to claim 3 comprising a sequence selected from the group consisting of SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 18, SEQ ID NO: 19 and SEQ ID NO: 132.

5. An immunomodulatory polynucleotide comprising an immunostimulatory sequence (ISS), wherein the ISS comprises the formula:

5'-X_1 X_2 A X_3 Z G X_4 T C G-3' (SEQ ID NO: 65)

wherein Z is 5-bromocytosine;

wherein X_1 is T, G, C or Z, wherein Z is 5-bromocytosine;

wherein X_2 is T, G, A or U;

wherein X_3 is T, A or C;

wherein X_4 is T, G or U; and

wherein the ISS is not 5'-TGAAZGTTCG-3' (SEQ ID NO: 66), wherein Z is 5-bromocytosine.

6. An immunomodulatory polynucleotide according to claim 5, wherein the ISS is selected from the group consisting of TGAAZGUTCG, (SEQ ID NO: 83) TGACZGTTCG (SEQ ID NO: 84), TGATZGGTCG (SEQ ID NO: 85), GTATZGGTCG (SEQ ID NO: 86), GTACZGTTCG (SEQ ID NO: 87), GAACZGTTCG (SEQ ID NO: 88), GAAAZGUTCG (SEQ ID NO: 89), ZGACZGTTCG (SEQ ID NO: 90), CGAAZGTTCG (SEQ ID NO: 91), ZGAAZGTTCG (SEQ ID NO: 92), ZGAAZGUTCG (SEQ ID NO: 93), TTAAZGUTCG (SEQ ID NO: 94), TUAAZGUTCG (SEQ ID NO: 95) and TTAAZGTTCG (SEQ ID NO: 96), wherein Z is 5-bromocytosine.

7. An immunomodulatory polynucleotide according to claim 6, wherein the ISS is selected from the group consisting of ZGAAZGUTCG (SEQ ID NO: 93) and GAAAZGUTCG (SEQ ID NO: 89), wherein Z is 5-bromocytosine.

8. An immunomodulatory polynucleotide according to claim 7 comprising a sequence selected from the group consisting of SEQ ID NO: 35 and SEQ ID NO: 36.

9. An immunomodulatory polynucleotide according to claim 1 or claim 5, wherein the immunomodulatory polynucleotide further comprises at least one TCG sequence.

10. An immunomodulatory polynucleotide according to claim 9, wherein the TCG sequence is adjacent to the 5' end of the ISS.

11. An immunomodulatory polynucleotide according to claim 1 or claim 5, wherein the immunomodulatory polynucleotide further comprises a TCGA sequence.

12. An immunomodulatory polynucleotide according to claim 1 or claim 5, wherein the immunomodulatory polynucleotide further comprises at least one T, 5-bromocytosine, G sequence.

13. An immunomodulatory polynucleotide according to claim 12, wherein the T, 5-bromocytosine, G sequence is adjacent to the 5' end of the ISS.

14. An immunomodulatory polynucleotide according to claim 1 or claim 5, wherein the immunomodulatory polynucleotide further comprises a T, 5-bromocytosine, G, A sequence.

15. An immunomodulatory polynucleotide according to claim 1 or claim 5, wherein the immunomodulatory polynucleotide is less than about 150 bases or base pairs in length.

16. An immunomodulatory polynucleotide according to claim 1 or claim 5, wherein the immunomodulatory polynucleotide is less than about 100 bases or base pairs in length.

17. An immunomodulatory polynucleotide according to claim 1 or claim 5, wherein the immunomodulatory polynucleotide is less than about 50 bases or base pairs in length.

18. An immunomodulatory polynucleotide according to claim 1 or claim 5, wherein the immunomodulatory polynucleotide is single-stranded.

19. An immunomodulatory polynucleotide according to claim 1 or claim 5, wherein the immunomodulatory polynucleotide is double-stranded.

20. An immunomodulatory polynucleotide according to claim 1 or claim 5, wherein the immunomodulatory polynucleotide is stabilized.

21. An immunomodulatory polynucleotide according to claim 20, wherein the polynucleotide comprises a phosphorothioate bond.

22. An immunomodulatory composition comprising an immunomodulatory polynucleotide according to claim 1 or claim 5.

23. An immunomodulatory composition according to claim 22 further comprising a pharmaceutically acceptable excipient.

24. An immunomodulatory composition according to claim 22 further comprising an antigen.

25. An immunomodulatory composition according to claim 24 further comprising a pharmaceutically acceptable excipient.

26. An immunomodulatory polynucleotide/microcarrier (IMP/MC) complex, comprising:

a polynucleotide according to claim 1 linked to a biodegradable microcarrier (MC), wherein said MC is less than 10 μm in size.

27. An immunomodulatory polynucleotide/microcarrier (IMP/MC) complex, comprising:

a polynucleotide according to claim 5 linked to a biodegradable microcarrier (MC), wherein said MC is less than 10 μm in size.

28. A method of modulating an immune response in an individual comprising administering to an individual an immunomodulatory polynucleotide according to claim 1 or claim 5 in an amount sufficient to modulate an immune response in said individual.

29. The method of claim 28, wherein said individual suffers from a disorder associated with a Th2-type immune response.

30. The method of claim 29, wherein said disorder associated with a Th2-type immune response is an allergy or asthma.

31. The method of claim 28, wherein said individual has an infectious disease.

32. A method of increasing interferon-gamma (IFN-γ) in an individual, comprising:

administering an immunomodulatory polynucleotide according to claim 1 or claim 5 to said individual in an amount sufficient to increase IFN-γ in said individual.

33. The method of claim 32, wherein said individual has idiopathic pulmonary fibrosis.

34. A method of increasing interferon-alpha (IFN-α) in an individual, comprising:

administering an immunomodulatory polynucleotide according to claim 1 or claim 5 to said individual in an amount sufficient to increase IFN-α in said individual.

35. The method of claim 34, wherein said individual has a viral infection.

36. A method of increasing interferon-alpha (IFN-α) in an individual, comprising:

administering an immunomodulatory polynucleotide according to claim 9 to said individual in an amount sufficient to increase IFN-α in said individual.

37. The method of claim 35, wherein said individual has a viral infection.

38. A method of increasing interferon-alpha (IFN-α) in an individual, comprising:

administering an immunomodulatory polynucleotide according to claim 11 to said individual in an amount sufficient to increase IFN-α in said individual.

39. The method of claim 38, wherein said individual has a viral infection.

40. A method of ameliorating a symptom of an infectious disease in an individual, comprising:

administering an effective amount of an immunomodulatory polynucleotide according to claim 1 or claim 5 to the individual, wherein an effective amount is an amount sufficient to ameliorate a symptom of said infectious disease.

41. The method of claim 40, wherein said infectious disease is an infectious disease caused by a cellular pathogen.

42. The method of claim 41, wherein said infectious disease caused by a cellular pathogen is selected from the group consisting of mycobacterial disease, malaria , leishmaniasis, toxoplasmosis, schistosomiasis and clonorchiasis.

43. A method of ameliorating a symptom of an IgE-related disorder in an individual, comprising:

administering an effective amount of an immunomodulatory polynucleotide according to claim 1 or claim 5 to an individual having an IgE-related disorder, wherein an effective amount is an amount sufficient to ameliorate a symptom of said IgE-related disorder.

44. The method of claim 43, wherein said IgE-related disorder is allergy.

45. The method of claim 43, wherein said IgE-related disorder is an allergy-related disorder.

46. The method of claim 43, wherein said IgE-related disorder is asthma.

47. A kit comprising an immunomodulatory polynucleotide according to claim 1 or claim 5.

48. The kit of claim 47, further comprising instructions for use of the immunomodulatory polynucleotide for immunodulation of an individual.